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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,022	09/17/2003	Dennis M. Klinman	4239-66899	7954

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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,022	KLINMAN ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 25-27* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, 23 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The action is responsive to communication filed 12/~~27~~12/2006. The status of the claims is as follows: claim 24 is canceled, claim 22 is drawn to a non-elected invention, and claims 1-21, 23 and 25-27 are under current examination. Applicants elected species SEQ ID NO: 1. BC 3/29/7

Applicant's election with traverse of Group I in the reply filed on 3/6/07 is acknowledged. The traversal is on the ground(s) that search for both Group I and II would not be an undue burden. This is not found persuasive because both groups are drawn to sequences with differential structures (K and D motifs or Formulas I and II as defined by the specification). Of note, the sequence set forth by SEQ ID NO: 20 has multiple variables which encompasses many, many different sequences.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections

35 U.S.C. 112, 1st paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 recites the limitation "anti-retroviral drug" in claim 2. There is insufficient antecedent basis for this limitation in the claim.

35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 7-8, 14-17, 21, 23 and 25-27 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application 10/502, 085 (hereinafter as "Jiang", 2002). The limitations of the rejected claims are as follows: a method of increasing an immune response to an infection in an immunocompromised subject, comprising administering an effective amount of an immunostimulatory D oligodeoxynucleotide; wherein the subject is infected with lentivirus, more specifically, HIV; wherein the ODN is at least 16 nucleotides in length; wherein the ODN is represented by the formula in claim 7; wherein the ODN comprises phosphodiester bases; wherein the ODN is self-complementary; wherein the infection is a bacterial, fungal or viral infection, more specifically, with *Leishmania*; wherein the infection includes candidiasis; wherein the ODN comprises the sequence set forth by SEQ ID NO: 1; wherein the antigenic epitope of a polypeptide is not administered to the subject; and wherein the ODN has the nucleic acid set forth by SEQ ID NO: 177.

Jiang discloses CpG oligonucleotides used as an immunostimulatory agent to protect against a disease caused by either a cancer cell or a pathogen, either alone or in conjunction with immunogens (see Abstract). Further, this reference discloses the sequence set forth by SEQ ID NO: 177 (see SEQ ID NO: 3, 20 amino acids in length).

As a result, this reference also teaches the sequence of SEQ ID NO: 1 which encompasses SEQ ID NO: 177 and the formula the instant specification defines in claim 7. Jiang teaches using phosphodiester linkages in the ODN (see for example, paragraph 218). Paragraph 141 recites the following regarding self-complementarity: "While the strands of a double stranded molecule are normally held together by noncovalent bonds (Watson-Crick base pairing as a result of hydrogen bonding), it is possible to stabilize the duplex by an internucleoside linkage which joins a 5' end of one strand to the proximal 3' end of the other strand (after which the ends in question are no longer free ends). This can be done with just one pair of ends, or with both of them. In like manner, a single stranded molecule which folds as a result of self-complementarity can have its folded structure stabilized by such a linkage. In either case, a lipophilic group may be incorporated into this linkage." Thus, all of the structural limitations are taught by the prior art. Jiang also teaches using his invention for treating diseases, including Leishmania, candidiasis and fungal and viral infections, including HIV (paragraph 285). Given all of the limitations have been met, these claims are rejected.

Claims 1-3, 7-8, 14-17, 21, 23 and 25-27 are rejected under 35 U.S.C. 102(e) as being anticipated by 09/874, 991 (hereinafter as "Mond").

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The limitations of the rejected claims are as follows: a method of increasing an immune response to an infection in an immunocompromised subject, comprising administering an effective amount of an immunostimulatory D oligodeoxynucleotide; wherein the subject is infected with lentivirus, more specifically, HIV; wherein the ODN is at least 16 nucleotides in length; wherein the ODN is represented by the formula in claim 7; wherein the ODN is self-complementary; wherein the infection is a bacterial, fungal or viral infection, more specifically, with *Leishmania*; wherein the infection includes candidiasis; wherein the ODN comprises the sequence set forth by SEQ ID NO: 1; wherein the antigenic epitope of a polypeptide is not administered to the subject; and wherein the ODN has the nucleic acid set forth by SEQ ID NO: 177.

Mond discloses immunostimulatory DNA, RNA and DNA/RNA hybrid oligonucleotides for generating an immune response. The sequence set forth by SEQ ID NO: 550 is 100% homologous to SEQ ID NO: 177 of the instant application. Of note, the claims are not limiting to either a DNA or RNA molecule and pyrimidines may encompass uracils. Mond also teaches that these ODN's may be used to treat a patient in need of immune stimulation (paragraph 54) and that they may be administered either

alone or co-administered with one or more antigens (Abstract). Infections disclosed by this reference include bacterial, fungal and viral (paragraph 72). More specifically, infections include HIV (paragraph 71), Leishmania (paragraph 76) and candida (paragraph 76). Paragraph 43 describes the use of phosphodiesters to render the ODN less susceptible to degradation. Lastly, according to paragraph 28 the ODN may encompass self-complementary structures. Thus, the claims above are rejected.

Claims 1, 7-17, 21, 23 and 25-27 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent # 6, 977, 245 (hereinafter as "Klinman").

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The limitations of the rejected claims are as follows: a method of increasing an immune response to an infection in an immunocompromised subject, comprising administering an effective amount of an immunostimulatory D oligodeoxynucleotide; wherein the ODN is at least 16 nucleotides in length; wherein the ODN is represented by the formula in claim 7; wherein the ODN comprises phosphodiester bases; wherein the ODN is self-complementary; wherein the infection is a bacterial, fungal or viral infection, more specifically, with *Leishmania*; wherein the infection includes candidiasis;

wherein the ODN comprises the sequence set forth by SEQ ID NO: 1; wherein the antigenic epitope of a polypeptide is not administered to the subject; and wherein the ODN has the nucleic acid set forth by SEQ ID NO: 177.

Klinman discloses the use of "D type CpG oligodeoxynucleotides" and a method of using these ODNs to induce an immune response (see Abstract). Further, the sequences set forth by SEQ ID NO: 177 and SEQ ID NO: 1 of the instant application is taught by SEQ ID NO: 1 of this prior art reference. These sequences include phoophodiester bases in both the CpG motif and its immediate flanking regions (see paragraph 94 and Table 1). Also see Table 1, for self-complementary sequences in bold. Infectious agents include viruses, bacteria and fungi (see paragraph 48) as well as Leishmania and hepatitis (see paragraph 135). Paragraph 129 describes administration of the ODN either alone or in combination with another molecule. Thus, Klinman meet the limitations of the rejected claims above.

35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jiang, Horner et al (2001) and Fraternale et al (2000). The limitations of the claims above are: a method of increasing an immune response to an infection in an immunocompromised subject, comprising administering an effective amount of an immunostimulatory D oligodeoxynucleotide; wherein the subject is immunocompromised as a result of a lentivirus, more specifically HIV-1 and HIV-2; wherein the subject has acquired AIDS; wherein the method further comprises HAART; and wherein the method further comprises AZT.

As discussed above, Jiang teaches administration of an ODN consisting of the sequence set forth by SEQ ID NO: 177 of the instant application. This ODN is used as an immunostimulatory agent to protect against a disease caused by either a cancer cell or a pathogen (see Abstract), including HIV (paragraph 285). This reference does not mention using such an ODN for the treatment of AIDS. Horner et al disclose immunostimulatory DNA-based vaccines that elicit multifaceted immune responses specifically against HIV (see Abstract). This reference also makes the following recitation: "these studies establish that ISS-based immunization elicits gp120-specific

cytokine, chemokine, and CTL responses from CD8 T cells in CD4 T cell-deficient mice, suggesting that this vaccination strategy could have clinical utility even in CD4 T cell-depleted AIDS patients for whom CD8 T cells are likely to play a crucial role in controlling infection" (see page 1589). While neither of the references above, explicitly express either HIV-1 or HIV-2, it is well known in the art that both viruses compromise the immune system as suggested by human immunodeficiency virus. Thus, it would have obvious to use an ODN in increasing immune responses in a subject who is infected with HIV-1 or HIV-2 as well as a subject who has acquired AIDS. One would have been motivated to stimulate the immune response with an ODN because of the teachings of Horner et al prove to be successful in eliciting multifaceted immune response against HIV (see entire document). Further, there would have been a reasonable expectation of success because the Horner et al provides a successful protocol and the underlying techniques are widely used in the art. The invention as whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

The above references do not disclose a method comprising administering HAART or AZT in combination with an ODN for subjects. Fraternale et al discusses the use of combination antiretroviral therapy in patients with HIV-1, including protease and reverse transcriptase inhibitors (see Abstract). This reference discloses that AZT is known for its anti-HIV-1 activity and has been shown to reduce progression of MAIDS. Also, this reference teaches that HAART produces a decline in plasma virus to undetectable levels in many patients (see Discussion). Thus, it would have been

obvious to one of ordinary skill in the art to combine either HAART or AZT with an ODN to further stimulate an immune response in a subject infected with HIV. One would have been motivated to do so, as suggest by Fraternale et al, because "patients entering these treatments are usually at advanced stages of the disease and have a poor immunologic status" (see page 219). There would have been a reasonable expectation of success given that the success of an ODN in eliciting immune responses against HIV is known as well as the success rate of both HAART and AZT in combating HIV. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

CONCLUSIONS

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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